

$X_1, X_2, X_m, X_{(m+1)}, X_{(2m-1)},$  and  $X_{2m}$  are carboxamide residues forming carboxamide binding pairs

$X_1/X_{2m}, X_2/X_{(2m-1)}, X_m/X_{(m+1)},$

$\gamma$  is  $\gamma$ -aminobutyric acid or 2,4 diaminobutyric acid, and

$R_1$  is  $-\text{NH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ ,  $-\text{NH}(\text{CH}_2)_{0-100}\text{CO NH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ , or  $-\text{NHR}_2$ , where  $R_2$  and  $R_3$

are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl,  $\text{C}_{1-100}$  alkyl,

$\text{C}_{1-100}$  alkylamine,  $\text{C}_{1-100}$  alkylaldiamine,  $\text{C}_{1-100}$  alkylcarboxylate,  $\text{C}_{1-100}$  alkenyl, a  $\text{C}_{1-100}$  alkynyl,

and  $\text{C}_{1-100}$  alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins,

polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports,

oligodeoxynucleotides, N-ethylnitrosourea, fluorescein, bromoacetamide, iodoacetamide, DL- $\alpha$ -

lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrinilic acid,

avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-

(psoraen-8-yloxy)-butyrate, taartaric acid, and (+)- $\alpha$ -tocopheral, suitable for use as a DNA-

binding ligand that is selective for identified target DNA-sequences  $5' - \text{WN}_1\text{N}_2 \dots \text{N}_m\text{W} - 3'$

where m is an integer having a value from 3 to 6, the method comprising:

(a) identifying a target sequence of double stranded DNA having the form  $5' - \text{WN}_1\text{N}_2 \dots \text{N}_m\text{W} - 3'$ ,  $\text{N}_1\text{N}_2 \dots \text{N}_m$  being the sequence to be bound by carboxamide residues, wherein each N is independently chosen from the group A, G, C, and T, each W is independently chosen from the group A and T, and m is an integer having a value from 3 to 6;

(b) representing the identified sequence as  $5' - \text{Wab} \dots \text{xW} - 3'$ , wherein a is a first nucleotide to be bound by the  $X_1$  carboxamide residue, b is a second nucleotide to be bound by the  $X_2$  carboxamide residue, and x is the corresponding nucleotide to be bound by the  $X_m$  carboxamide residue;

(c) defining  $a$  as A, G, C, or T to correspond to the first nucleotide to be bound by a carboxamide residue in the identified sequence;

(d) selecting Im as the  $X_1$  carboxamide residue and Py as the  $X_{2m}$  carboxamide residue if  $a = G$ ;

(e) selecting Py as the  $X_1$  carboxamide residue and Im as the  $X_{2m}$  carboxamide residue if  $a = C$ ;

(f) selecting Hp as the  $X_1$  carboxamide residue and Py as the  $X_{2m}$  carboxamide residue if  $a = T$ ;

(g) selecting Py as the  $X_1$  carboxamide residue and Hp as the  $X_{2m}$  carboxamide residue if  $a = A$ ; and

(h) repeating steps c - g for  $b$  through  $x$  until all carboxamide residues are selected;

wherein Im is N-methylimidazole, Hp is , Py is N-methylpyrrole, A is adenine, G is guanine, C is cytosine, and T is thymine.

2. (Amended) The method of claim 1 further comprising the step of synthesizing the polyamide.

3. (Amended) The method of claim 2 further comprising the step of determining if the binding affinity of the polyamide to the identified target sequence is subnanomolar.

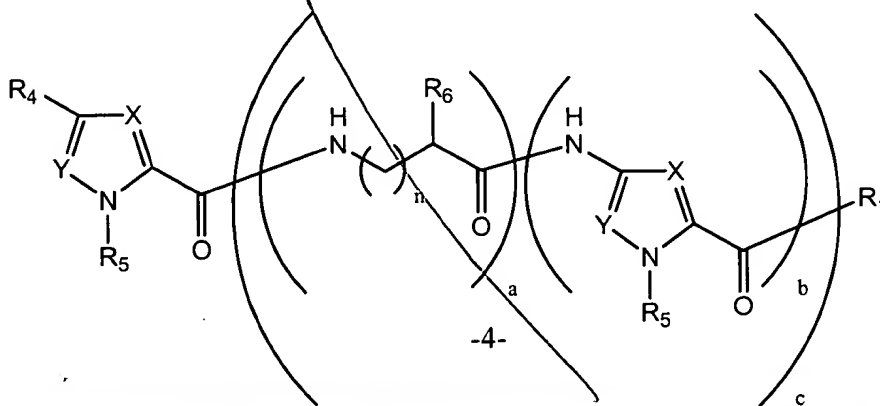
4. (Amended) The method of claim 1 further comprising the step of determining if the polyamide exhibits a binding affinity that is at least ten-fold higher for said identified target sequence compared to a non-target DNA sequence.

38. (Amended) A polyamide composition produced by the method of claim 2 wherein one carboxamide binding pair is  $\beta/\beta$ , wherein  $\beta$  is  $\beta$ -alanine.

42. (Amended) The method of claim 1 wherein the identified target DNA sequence is a regulatory sequence.
43. (Amended) The method of claim 1 wherein the identified target DNA sequence is a promoter sequence.
44. (Amended) The method of claim 1 wherein the identified target DNA sequence is a coding sequence.
- ①<sup>3</sup> 45. (Amended) The method of claim 1 wherein the identified target DNA sequence is a non-coding sequence.
46. (Amended) A polyamide composition produced by the method of claim 2 wherein the binding of the carboxamide binding pairs to the identified target DNA sequence modulates the expression of a gene.
47. (Amended) A composition comprising an effective amount of a polyamide produced by the method of claim 2 and a pharmologically suitable excipient.
48. (Amended) A diagnostic kit comprising a polyamide produced by the method of claim 2.

Please enter the following new claim:

49. (New) A polyamide designed by the method of claim 1, having the structure:



wherein

$R_4$  is selected from the group consisting of H,  $NH_2$ , SH, Cl, Br, F, N-acetyl, and N-formyl;

each  $R_5$  is independently selected from the group consisting of H,  $(CH_2)_{0-6}CH_3$ ,  $(CH_2)_{0-6}NH_2$ ,  $(CH_2)_{0-6}SH$ ,  $(CH_2)_{0-6}OH$ ,  $(CH_2)_{0-6}N(R_7)_2$ ,  $(CH_2)_{0-6}OR_7$ , and  $(CH_2)_{0-6}SR_7$ , wherein  $R_7$  is  $(CH_2)_{0-6}CH_3$ ,  $(CH_2)_{0-6}NH_2$ ,  $(CH_2)_{0-6}SH$ , or  $(CH_2)_{0-6}OH$ ;

each  $R_6$  is independently selected from the group consisting of H,  $NH_2$ , OH, SH, Br, Cl, F, OMe,  $CH_2OH$ ,  $CH_2SH$ , and  $CH_2NH_2$ ;

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 $R_1$  is  $-NH(CH_2)_{0-100}NR_2R_3$ ,  $-NH(CH_2)_{0-100}CO NH(CH_2)_{0-100}NR_2R_3$ , or  $-NHR_2$ , where  $R_2$  and  $R_3$  are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl,  $C_{1-100}$  alkyl,  $C_{1-100}$  alkylamine,  $C_{1-100}$  alkyldiamine,  $C_{1-100}$  alkylcarboxylate,  $C_{1-100}$  alkenyl, a  $C_{1-100}$  alkynyl, and  $C_{1-100}$  alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosourea, fluorescein, bromoacetamide, iodoacetamide, DL- $\alpha$ -lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthranilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, tartaric acid, and (+)- $\alpha$ -tocopherol;

each X and Y are independently selected from the group consisting of N, CH, COH,  $CCH_3$ ,  $CNH_2$ , CCl, and CF;

each n is an integer from 1 to 2;

each a is an integer from 0 or 1;